



CHUV team members examine a ^{177}Lu xSPECT Quant image.

Defining the quantitative future of SPECT/CT

SPECT/CT imaging, with its innate ability to detect and characterize abnormalities in their earliest forms, is a meaningful tool for determining prompt diagnoses and developing personalized treatment strategies. Such a tool is invaluable as we move toward precision medicine, and the significant addition of reliable quantitative measurements only enhances SPECT/CT's opportunities. But as quantitative SPECT/CT looks to establish an active role in the next era of healthcare, the extent of its impact continues to be defined.

While the concept of quantitative SPECT/CT has existed for years, SPECT/CT systems are not intrinsically quantitative; their means for measuring activity concentration are limited without additional efforts such as manual, complex calibrations. While publications stress the benefits of quantification, they simultaneously reinforce the importance of accuracy by sharing tips for more easily obtaining measurements and minimizing chances for error.

These obstacles are far less discouraging now that technologies are in place to address them. Today's automated measurement tools allow us to go beyond questioning whether quantitative SPECT/CT will impact the future of medicine and instead ask how much of an impact it will have.

As we evaluate how quantitative SPECT/CT will influence care, the emphasis remains on the validation of:

- how quantification can be utilized in routine care paths
- the contribution to a more precise diagnosis
- the value in treatment management.

Around the world there are now individuals and teams who drive this debate, with the ultimate goal of reaching a consensus within the scientific community. One such team resides in the nuclear medicine and molecular imaging department at Centre Hospitalier Universitaire Vaudois (CHUV), situated on the shores of Lake Geneva in Lausanne, Switzerland.

Simplifying quantification

Over the past decade, the team at CHUV devoted a portion of their work to better understand the potential, and constraints, of SPECT/CT quantification. While applying quantitative SPECT/CT in select therapeutic situations, they identified the opportunity for more diagnostic and treatment applications. Simultaneously, they recognized the potential benefits of incorporating quantitative SPECT/CT as a standard imaging practice. Yet, without a simplified way to obtain reliable and accurate quantitative results, their progress toward routine, clinical implementation was difficult.

"Ten years ago, it was very complicated. We had to have technicians and

medical physicists do the calibration to have an equivalence of how many megabecquerel were making how many counts. So, we had to establish a standard with a known activity and a known volume. From the imaging, we could then derive how many counts equal how many megabecquerel," recalls John Prior, MD, PhD, FEBNM, head of nuclear medicine at CHUV.

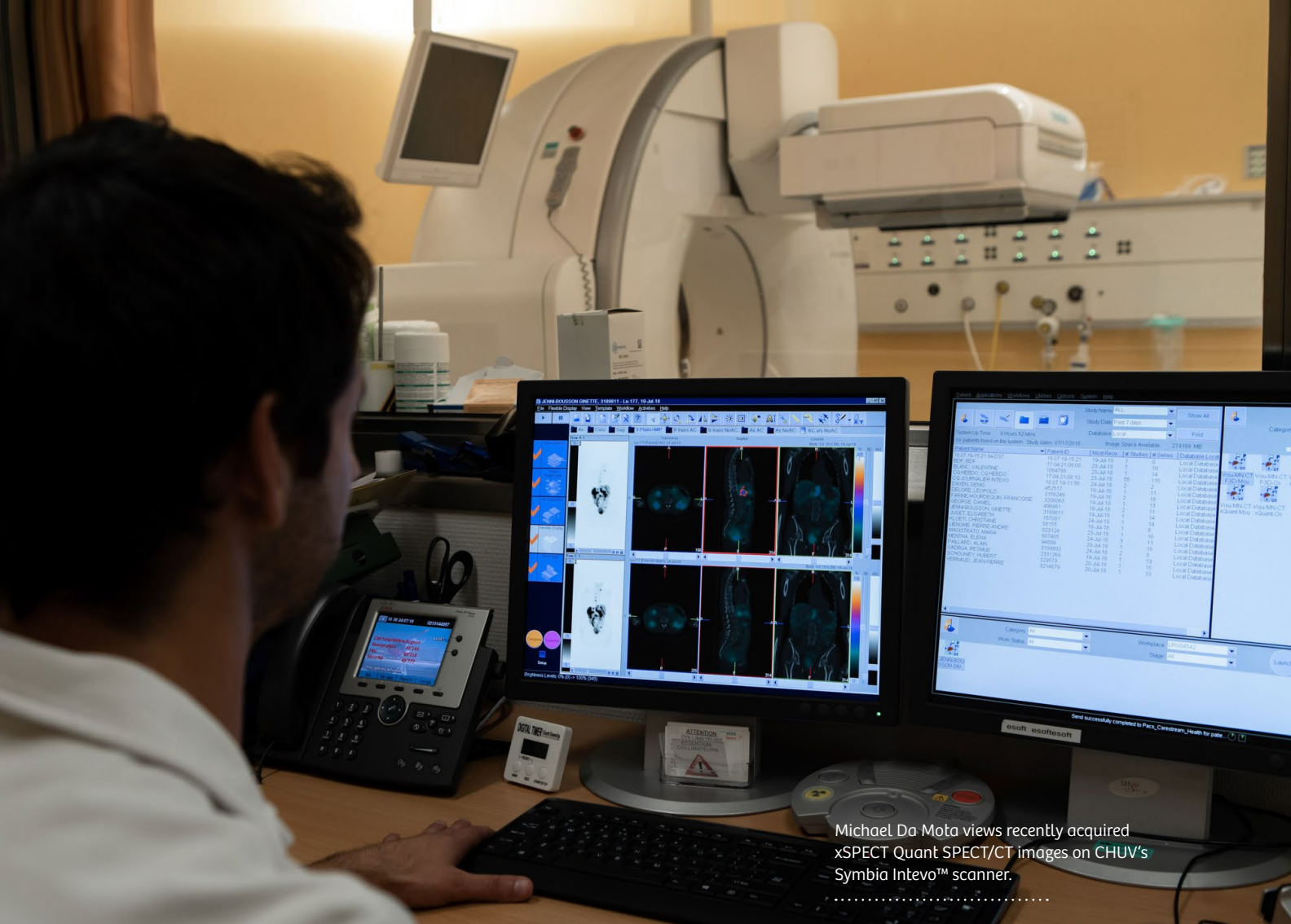
In 2014, Prior and his team adopted technology that was able to assist them as they forged a path towards routine quantification in SPECT/CT. With the installation of xSPECT Quant™, CHUV began to apply this new form of automated quantification in their Technetium-99m (^{99m}Tc) SPECT/CT studies. In 2016, their quantification work expanded to other isotopes, such as Iodine-123 (^{123}I), Indium-111 (^{111}In), and Lutetium-177 (^{177}Lu).

When referencing xSPECT Quant, Prior asserts, "it's done automatically, so the machine is intrinsically quantitative. In everyday SPECT/CT, we now get this valuable quantitative information with much less effort."

"Before, our number of quantitative procedures were just a few because



Prior, Da Mota, and Gnesin (pictured left to right) gather around CHUV's workstations to assess recent quantitative SPECT/CT images.



Michael Da Mota views recently acquired xSPECT Quant SPECT/CT images on CHUV's Symbia Intevo™ scanner.

we calibrated the system only for specific patients,” admits Silvano Gnesin, PhD, a medical physicist at CHUV. “But since it is easier to obtain absolute quantification, most of our SPECT/CT procedures are quantitative.”

“We do a lot more SPECT/CT than before, because of the quantification that goes with it,” affirms Michael Da Mota, technologist in charge of molecular therapy at CHUV. “We now have doctors that write xSPECT Quant in their examination demands.” Referring to the pressure to keep up with the increase in studies, Da Mota jokes, “we have to run a little bit more to schedule all the patients.”

Demonstrating the diagnostic value

CHUV's work includes evaluating the utility of quantitative SPECT/CT in diagnosis. “We are now using xSPECT quantification in our clinical routine,” states Mario Jreige, MD, radiologist and nuclear medicine resident at CHUV. “We often have cases that are borderline, where visual interpretation is limited. Quantification helps us get a more precise diagnosis,” he explains. “One of the cases we communicated in an abstract at the 2018 Society of Nuclear Medicine and Molecular Imaging (SNMMI) meeting is where the patient had changes in the vertebrae and was referred for staging.

Based on the SUV, it was clear the lesion had very low uptake and tended more towards osteoarthritis, rather than metastatic disease.”

“If physicians do not have quantitative SUV measurements, they look at the darkness in an image and when it's really, really dark they say, ‘Well, it's probably metastatic,’” adds Prior. “We made some first measurements with ^{99m}Tc bone scans and it looks like everything that has an SUV higher than 20 would be more metastatic and everything that stays below 20 would be more degenerative disease. With SUV we can characterize with more certainty a lesion that has an SUV of 15 or 25 and, for the patient, it makes a lot of difference.”



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Niklaus Schaefer, MD, Centre Hospitalier Universitaire Vaudois

"It is important for us to define criteria because this will lead to very accurate diagnostic capabilities for examinations," Prior points out. "This will help patients to have their diagnoses earlier, and with more precision," underscores Jreige.

When questioned on their impressions of the technology, Prior replies, "we've had many 'aha moments,' with xSPECT quantification. One example was when we were able to quantify the uptake from the striatum in patients with potential Parkinson's disease. We know we can see this, and usually also do a ratio between the striatum and the occipital region. It's very technical, but it's a way of getting an index of normality. So having an absolute value, and not needing to make a ratio, was something we found interesting and thought maybe, with this, we can catch disease earlier."

Building off the interest generated by their findings, Prior and team designed an ^{123}I xSPECT Quant study to compare the absolute quantification with conventional relative analysis. Also presented at SNMMI 2018, their results indicate absolute quantification is capable of measuring direct activity and reflecting slight differences between the pathological and non-pathological patient population, which they believe can help define disease earlier.

"In my opinion, physicians are more and more confident as they

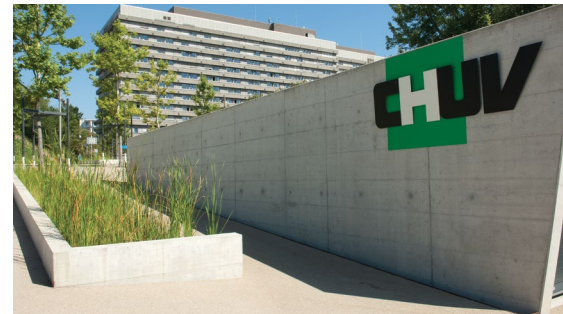
use xSPECT Quant. We are moving towards a future where quantification is standard," Gnesin reflects when asked about the potential for routine clinical use.

Advancing therapy outcomes

Beyond diagnostics, the team at CHUV spends considerable time investigating the influence quantitative SPECT/CT has on therapy planning and assessment. "We are trying to tailor each treatment, and quantitative imaging with SPECT allows us to get more precise information about how to do it better for each patient," shares Prior. Currently, CHUV applies quantitative SPECT/CT to their ^{177}Lu and Iodine-131 (^{131}I) studies, both of which appear to hold promise.

"I think it's significant that we are not just judging on gray stuff appearing on images. It's important that we deliver numbers, because one of the key points to treating disease is to really measure the degree of disease and treatment response," stresses Niklaus Schaefer, MD, a nuclear medicine physician at CHUV.

For therapy monitoring Schaefer conveys, "after the second cycle of treatment, we want to be sure the patient is responding. First, it really helps the patient to understand



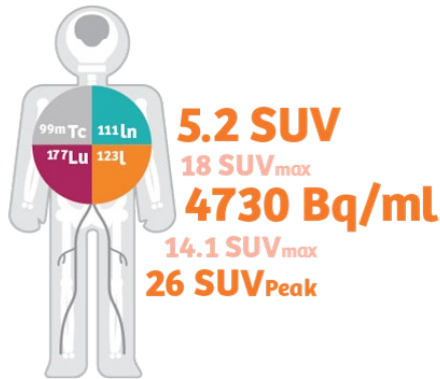
A glance at CHUV

CHUV, an institution that leads the way in SPECT/CT quantification research and clinical implementation, is one that:

- performs 8,400 molecular imaging studies a year
 - nearly half are SPECT-based exams.
- utilizes a Symbia Intevo with xSPECT Quant to perform their SPECT/CT quantification studies.
- employs a staff of:
 - three senior physicians
 - three fellows and three residents
 - 15 technologists
 - two clinical radiopharmacists
 - one medical physicist.
- participates in several research collaboration efforts centered around:
 - radiopharmaceutical development for diagnosis and therapy
 - medical physics for quantitative imaging and dosimetry.

What is xSPECT Quant?

xSPECT Quant



Introduced in 2013, xSPECT Quant was the first solution capable of delivering absolute SPECT/CT quantification that allows for accurate, reproducible, and standardized quantitative clinical studies.

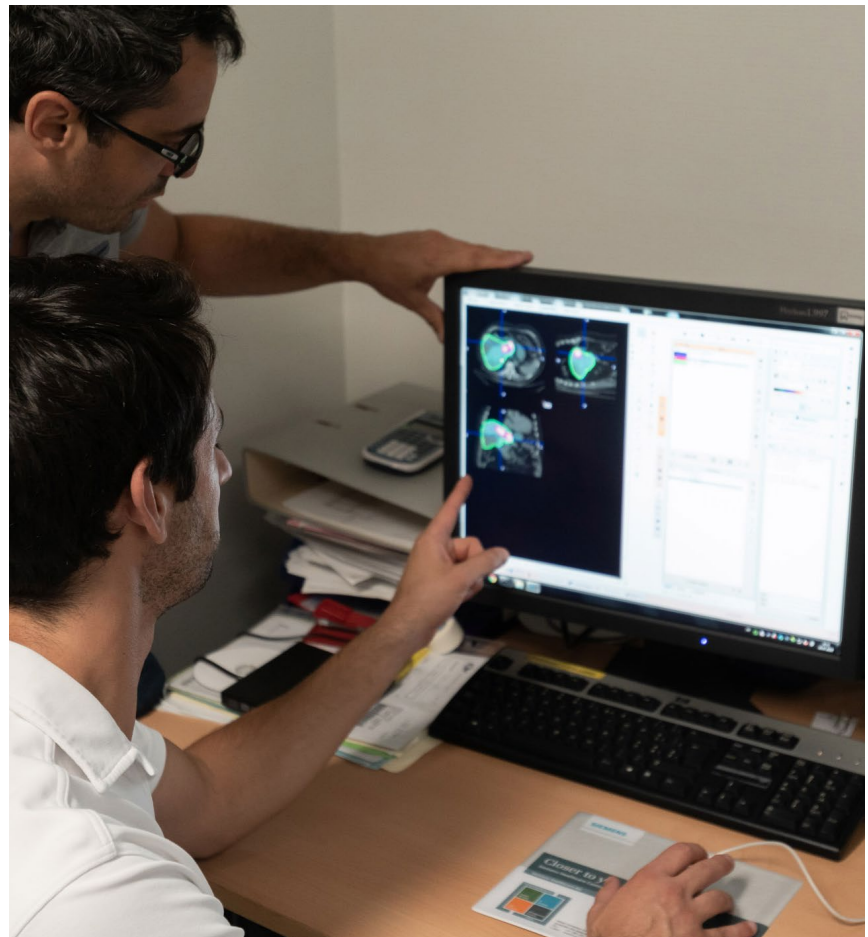
xSPECT Quant uses a patented calibrated sensitivity source, traceable to the National Institute of Standards and Technology (NIST) to standardize system sensitivity, which enables comparable quantitative results. This ability leads to consistency across systems and time, with quantification that is independent of patient variability.

Accurate to within 5%^[a], xSPECT Quant continues to be the industry's most precise and reproducible SPECT/CT quantitative solution.

what's happening and second, we know if the treatment is effective." Schaefer further explains, "in some cases, I see almost exactly the same image after four cycles so it's very important to measure if there is any difference. When you treat a patient with neuroendocrine tumors and see that the lesions are still there, you may think there's no response. But once you measure and quantify your images, you start to understand that that they are responding quite well with 10, 20, or even more percent reduction."

However, Schaefer acknowledges this evaluation is an ongoing process. "We need to better understand what these figures mean. We have to be able to tell if a reduction of 10% is meaningful or not. These figures need to be put into context with real clinical outcomes." Reinforcing this sentiment, Prior adds, "we need to design more studies to see where and how SPECT/CT quantification can help us. We have many ideas, we're doing research, and we're writing protocols."

When considering upcoming applications, Prior shares, "it's a tricky question but I think it's really



Gnesin and Da Mota utilize xSPECT Quant images to plan therapy.

Schaefer, Prior, and Jreige gather around CHUV's Symbia Intevo SPECT/CT scanner.



a breakthrough that xSPECT Quant can be performed with ^{177}Lu , because many of our future therapies will be done with this isotope.” Jreige highlights that they anticipate testing PSMA-Lutetium targeted therapy for prostate cancer patients.^[b] “We want to see if we can adjust the doses of therapy based on the initial quantification of the tracer.”

As CHUV and others continue to explore and share their insights, we come closer to understanding the value of SPECT/CT quantification in diagnostics and therapy management. Fortunately, as evidence mounts, so does enthusiasm for molecular quantitative imaging becoming the gateway to precision medicine. ●

^[a] Data on file.

^[b] ^{177}Lu PSMA is not currently recognized by the U.S. Food and Drug Administration (FDA) or other regulatory agencies as being safe and effective. Siemens Healthineers does not make any claims regarding its use.

The statements by Siemens Healthineers' customers described herein are based on results that were achieved in the customer's unique setting. Since there is no “typical” hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.

xSPECT Quant is not commercially available in some countries. Due to regulatory reasons, its future availability cannot be guaranteed. Please contact your local Siemens organization for further details.

Join us

Our upcoming series of articles and podcasts explore CHUV's journey to uncover the quantitative future of SPECT/CT.

- 1) Utilizing different isotopes with xSPECT Quant
- 2) Modern quantitative SPECT/CT and the changing role of the nuclear medicine physicist
- 3) The impact of SPECT/CT quantification on therapy

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